Are cardiovascular adverse events with Ibrutinib well considered?

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**Background**
- Chronic lymphocytic leukemia and mantle cell lymphoma have a new standard of care:
  - **Ibrutinib** (metabolized by CYP 3A4/5 and P-glycoprotein inhibitor)
  - Cardiovascular (CV) adverse events are known with **atrial fibrillation** (AF) (5-13.8%), **bleeding event** (BE) (grade 3 or 4 about 3-4%), **hypertension**
- CV pre-treatment evaluation is not required in Ibrutinib summary of product characteristics (SPC)

**Objectives**
- Evaluate whether the CV risks are considered regarding the prescription of Ibrutinib
- Measure cardiovascular adverse event occurrence during treatment

**Results**
- 55 medical records were analyzed
- The patient’s mean age was 70 years old
- **Risk factors evaluation**
  - 65% had at least one CV risk factor
  - 5 patients had more than 3 CV risk factor
- **38% had CV monitoring during their treatment**
- **25% had at least one initial cardiac exam (ECG/Holter, echocardiography, cardiology consultation)**
- **One patient had myocardial infarction**
- **3 patients developed hypertension**

**Material and Methods**
A retrospective analyze was conducted including patients with Ibrutinib initiation in our hematology department from May 2014 to July 2017. A database was constituted consulting all the medical records including:
- demographic, clinical and biological informations
- adverse events
- CV evaluation
- potential drug interactions
The incidence of AF and BE and the CHA2DS2-VASc score were calculated

**Discussion**
- Our results show that cardiac pre-treatment exam are few performed (25%) despite our patients CV risk factors
- With 7.2% of AF, this risk is not negligible considering the limited cohort
- Almost half (44%) of patients presented BE. A part of serious BE could have been prevented, as concomitant drugs, especially CYP 3A4 inhibitors, seems to play a role in CV adverse event occurrence. Patients are all the more exposed at BE because of their comorbidities can require anti-platelet medication.

**Conclusion**
The therapeutic management of adverse event seems to be not standardized. As a result of drug interactions and CV consequence, which can lead to serious outcomes, a multidisciplinary consultation including hematologist, cardiologist and pharmacist should be established at the initiation and during treatment by Ibrutinib.

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